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Comments:

Proposed Interview agenda (including proposed claim amendments and one reference) for discussion on December 18, 2003 1:30pm (EST)

U.S. Application No. 09/636,530

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sd-176491

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In re Patent Application of: Thomas L. CANTOR	
Application No.: 09/636,530	Art Unit: 1646
Filed: August 10, 2000	Examiner: Dong Jiang
For: PARATHYROID HORMONE ANTAGONISTS OR MODULATORS AND USES THEREFOR	

INTERVIEW AGENDA - 12/18/03

Issue 1 (New Matter): Whether claim 14, directed to a PTH antagonist composition with an N-terminus starting at any position spanning from 8 through 34 of SEQ ID NO: 1 is supported in the specification.

Our position: (1) Amended claim 14 is supported at, *e.g.*, pg 1, lns 8-12; pg 4, lns 4-13; pg 5, lns 23-26; and sequence listing; (2) the claimed antagonist falls within the original described and claimed range; (3) multiple examples (*e.g.*, PTH_{9-84}, PTH_{28-84} and PTH_{34-84}) are provided within the range (*see, e.g.*, pg 1, lns 10-11; pg 4, lns 5-6; and pg 5, lns 23-26); and (4) legal support for our position can be found, *e.g.*, in *In re Wertheim*, 191 USPQ 90 (CCPA 1976); *In re Driscoll*, 195 USPQ 434, 437-38 (CCPA 1977); MPEP § 2163.05 (range limitations); and *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1321 (Fed. Cir. 2003) (acknowledging the test for sufficiency of support in an application is whether an artisan would recognize possession as set out in the disclosure).

Issue 2 (Anticipation): (1) Whether *Takasu* anticipates claims 14 and 16; and (2) whether *Fukuda* anticipates claims 22-25 and 30-33.

Our positions: *Takasu* - *Takasu's* mutein consists of hPTH (35-84); but the claims require an N-terminus spanning between positions 8 and 34, and a C-terminus at 84. Thus, all limitations are not present in *Takasu*. anticip. b)

Fukuda - (1) In contrast to the present claims, *Fukuda's* muteins stimulate adenylate cyclase activity (ACA), as evidenced by the measured mutein-stimulated ACA-linked cAMP levels (*see Fukuda* "Experimental Example" page 23; and Shigeno *et al.* (included herewith and cited in the *Fukuda* Example)); and (2) no indication that any of *Fukuda's* thousands of muteins have "antagonistic" activity in accordance with the current claims.

Issue 3 (Obviousness): Whether claims 26-29 and 34-38 are rendered obvious by *Fukuda* and *Kanmera*.

Our position: *Fukuda* (see above). *Kanmera* - With regard to the adynelate cyclase activity of *Fukuda's* and *Kanmera's* muteins, even when taken together, the references do not teach the present claim limitations (*see* above and *Kanmera* at pages 8-10). Further, *Kanmera* appears to teach PTHrP substituted derivatives and teaches away from the use of: (1) truncated PTH or PTHrP fragments as they lack the desired "activity levels"; and (2) substituted PTH or PTHrP fragments as they lack predictable activity. *See, e.g.*, pg 2, lns 47-58. Each of *Fukuda's* muteins tested for "antagonistic" activity were substituted, thus no reasonable expectation of success seems present if combined with *Kanmera*.

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Proposed Claim Amendments

Claims 1-13 (Cancelled)

14. **(Proposed Amendment - For Discussion Only)** A pharmaceutical parathyroid hormone (PTH) antagonist composition, wherein the PTH antagonist composition comprises a peptide exhibiting PTH antagonist activity, together with a pharmaceutical carrier or excipient, wherein the PTH antagonist comprises a contiguous portion of human PTH having an amino acid sequence set forth in SEQ ID NO:1 (PTH_{1-84}), and ~~that~~ has the following characteristics:

a) the N-terminal amino acid residue of the PTH antagonist starts at any position spanning from position 8 through position 34 of SEQ ID NO:1 (PTH_{1-84}); and

b) the C-terminal amino acid residue of the PTH antagonist ends at position 84 of SEQ ID NO:1 (PTH_{1-84}).

Claim 15 (Cancelled)

16. (Previously amended) The antagonist of claim 14, wherein the PTH antagonist is selected from the group consisting of SEQ ID NO:5 (PTH_{28-84}) and SEQ ID NO:3 (PTH_{54-84}).

Claims 17-21 (Cancelled)

22. **(Proposed Amendment - For Discussion Only)** A method for treating a patient having hyperparathyroidism comprising administering to a patient having hyperparathyroidism a PTH antagonist peptide exhibiting PTH antagonist activity, ~~which antagonist activity comprises decreasing the *in vivo* calcium ion concentration in the blood of the patient or countering hypercalcemia;~~ wherein said PTH antagonist peptide avoids stimulating adenylate cyclase activity, in a therapeutically effective, but non-toxic amount, wherein the PTH antagonist comprises a contiguous portion of human PTH having an amino acid sequence set forth in SEQ ID NO:1 (PTH_{1-84}), and ~~that~~ has the following characteristics:

a) the N-terminal amino acid residue of the PTH antagonist starts at any position spanning from position 2 through position 34 of SEQ ID NO:1 (PTH_{1-84}); and

b) the C-terminal amino acid residue of the PTH antagonist ends at position 84 of SEQ ID NO:1 (PTH_{1-84}).

23. (Previously presented) The method of claim 22, wherein the N-terminal amino acid residue of the PTH antagonist starts at any position spanning from position 3 through position 28 of SEQ ID NO:1 (PTH_{1-84}), and the C-terminal amino acid residue of the PTH antagonist ends at position 84 of SEQ ID NO:1 (PTH_{1-84}).

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24. (Previously presented) The method of claim 22, wherein the PTH antagonist is selected from the group consisting of SEQ ID NO:2 (PTH_{2-84}), SEQ ID NO:4 (PTH_{3-84}), SEQ ID NO:5 (PTH_{28-84}), and SEQ ID NO:3 (PTH_{34-84}).

25. (Previously presented) The method of claim 22, wherein the PTH antagonist is administered together with a pharmaceutical carrier or excipient.

26. **(Proposed Amendment - For Discussion Only)** A method for treating a patient having renal osteodystrophy comprising administering to a patient having renal osteodystrophy a PTH antagonist peptide exhibiting PTH antagonist activity, ~~which antagonist activity comprises decreasing the *in vivo* calcium ion concentration in the blood of the patient or countering hypercalcemia,~~ wherein said PTH antagonist peptide avoids stimulating adenylate cyclase activity, in a therapeutically effective, but non-toxic amount, wherein the PTH antagonist comprises a contiguous portion of human PTH having an amino acid sequence set forth in SEQ ID NO:1 (PTH_{1-84}), and ~~that~~ has the following characteristics:

a) the N-terminal amino acid residue of the PTH antagonist starts at any position spanning from position 2 through position 34 of SEQ ID NO:1 (PTH_{1-84}); and

b) the C-terminal amino acid residue of the PTH antagonist ends at position 84 of SEQ ID NO:1 (PTH_{1-84}).

27. (Previously presented) The method of claim 26, wherein the N-terminal amino acid residue of the PTH antagonist starts at any position spanning from position 3 through position 28 of SEQ ID NO:1 (PTH_{1-84}), and the C-terminal amino acid residue of the PTH antagonist ends at position 84 of SEQ ID NO:1 (PTH_{1-84}).

28. (Previously presented) The method of claim 26, wherein the PTH antagonist is selected from th group consisting of SEQ ID NO:2 (PTH_{2-84}), SEQ ID NO:4 (PTH_{3-84}), SEQ ID NO:5 (PTH_{28-84}), and SEQ ID NO:3 (PTH_{34-84}).

29. (Previously presented) The method of claim 26, wherein the PTH antagonist is administered together with a pharmaceutical carrier or excipient.

30. **(Proposed Amendment - For Discussion Only)** A method for *in vivo* decreasing calcium ion concentration in blood of a subject comprising administering to a subject a PTH antagonist peptide exhibiting PTH antagonist activity, ~~which antagonist activity comprises decreasing the *in vivo* calcium ion concentration in the blood of the subject or countering hypercalcemia,~~ wherein said PTH antagonist peptide avoids stimulating adenylate cyclase activity, in [[a]] an effective, but non-toxic amount, wherein the PTH antagonist comprises a

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Proposed Claim Amendments

contiguous portion of human PTH having an amino acid sequence set forth in SEQ ID NO:1 (PTH_{1-84}), and ~~that~~ has the following characteristics:

a) the N-terminal amino acid residue of the PTH antagonist starts at any position spanning from position 2 through position 34 of SEQ ID NO:1 (PTH_{1-84}); and

b) the C-terminal amino acid residue of the PTH antagonist ends at position 84 of SEQ ID NO:1 (PTH_{1-84}).

31. (Previously presented) The method of claim 30, wherein the N-terminal amino acid residue of the PTH antagonist starts at any position spanning from position 3 through position 28 of SEQ ID NO:1 (PTH_{1-84}), and the C-terminal amino acid residue of the PTH antagonist ends at position 84 of SEQ ID NO:1 (PTH_{1-84}).

32. (Previously presented) The method of claim 30, wherein the PTH antagonist is selected from th group consisting of SEQ ID NO:2 (PTH_{2-84}), SEQ ID NO:4 (PTH_{3-84}), SEQ ID NO:5 (PTH_{28-84}), and SEQ ID NO:3 (PTH_{34-84}).

33. (Previously presented) The method of claim 30, wherein the PTH antagonist is administered together with a pharmaceutical carrier or excipient.

34. **(Proposed Amendment - For Discussion Only)** A method for treating a patient having osteoporosis comprising administering to a patient having osteoporosis a PTH antagonist peptide exhibiting PTH antagonist activity, ~~which antagonist activity comprises decreasing the *in vivo* calcium ion concentration in the blood of the patient or countering hypercalcemia,~~ wherein said PTH antagonist peptide avoids stimulating adenylate cyclase activity, in a therapeutically effective, but non-toxic amount, wherein the PTH antagonist comprises a contiguous portion of human PTH having an amino acid sequence set forth in SEQ ID NO:1 (PTH_{1-84}), and ~~that~~ has the following characteristics:

a) the N-terminal amino acid residue of the PTH antagonist starts at any position spanning from position 2 through position 34 of SEQ ID NO:1 (PTH_{1-84}); and

b) the C-terminal amino acid residue of the PTH antagonist ends at position 84 of SEQ ID NO:1 (PTH_{1-84}).

35. (Previously presented) The method of claim 34, wherein the N-terminal amino acid residue of the PTH antagonist starts at any position spanning from position 3 through position 28 of SEQ ID NO:1 (PTH_{1-84}), and the C-terminal amino acid residue of the PTH antagonist ends at position 84 of SEQ ID NO:1 (PTH_{1-84}).

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36. (Previously presented) The method of claim 34, wherein the PTH antagonist is selected from the group consisting of SEQ ID NO:2 (PTH_{2-84}), SEQ ID NO:4 (PTH_{3-84}), SEQ ID NO:5 (PTH_{28-84}), and SEQ ID NO:3 (PTH_{34-84}).

37. (Previously presented) The method of claim 34, wherein the PTH antagonist is administered together with a pharmaceutical carrier or excipient.

38. (Previously presented) The method of claim 34, wherein the PTH antagonist administration is either in a continuous or in a pulsatile manner.